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OFFICE OF THE SECRETARY
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SECNAVINST 3900.39C
ONR 34
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SECNAV INSTRUCTION 3900.39C

From: Secretary of the Navy
To: All Ships and Stations

Subj: PROTECTION OF HUMAN SUBJECTS

Ref: (a) 32 Code of Federal Regulations 219
(b) 45 Code of Federal Regulations 46
(c) DoD Directive 3216.2 of 7 Jan 83 (NOTAL)
(d) 5 United States Code 3109
(e) SECNAVINST 5212.5D, Navy and Marine Corps Records Disposition Manual, Section 3900, Paragraph 5, Page III-3-63 of 22 Apr 98
(f) 10 United States Code 980
(g) SECNAVINST 5211.5D, Department of the Navy Privacy Act (PA) Program, 10(a) Page 12, 10(d) Page 13 of 17 July 92
(h) 21 Code of Federal Regulations 50 and 56

Encl: (1) Definitions

1. Purpose. To prescribe policy and assign responsibility concerning the use and protection of human subjects and assurance of their personal privacy rights in studies conducted by, within, or for the Department of the Navy (DON) per references (a) through (h).

2. Cancellation. SECNAVINST 3900.39B. This instruction has been extensively rewritten and should be read in its entirety.

3. Scope

a. This instruction applies to the use of human subjects:

(1) In all research conducted by naval activities or personnel, or supported by naval activities through any agreement (e.g., contract, grant, cooperative agreement, or other arrangement), regardless of the source of funding or site of performance.

(2) In the development, testing or evaluation of any item, system, vehicle, aircraft, piece of equipment or other materiel, even if a person is not the direct object of the research. Examples include training exercises associated with

the testing of personal protective equipment when worn by a person and the study of a new clinical laboratory test requiring freshly drawn blood.

b. This instruction does not apply to:

(1) Efforts determined to be exempt per Section 101(b) of reference (a). For determination of exempt research, see paragraph 7g(1) of this instruction.

(2) Professionals who are specifically qualified by training and experience to perform some hazardous duty while they are acting within the scope of those duties, such as, but not limited to, test pilots or experimental divers. However, these professionals are not categorically exempt from this instruction. If these professionals are enrolled as subjects in studies that are not specifically included in their professional duties, regardless of whether such studies are collateral or entirely unrelated to their routine duties, this instruction applies.

(3) Provision of commercial services or other non-collaborative services that do not produce results that either merit professional recognition or publication.

c. This instruction shall not be suspended or waived:

(1) Due to operational contingency or

(2) During times of national emergency, except by explicit action of higher authority.

d. Nothing in this instruction is intended to supersede either the requirements for health or safety reviews required by other authority, or the authority of a health care practitioner to provide emergency medical care.

4. Background. The use of humans as research subjects has received considerable national and international attention in recent years. Many studies conducted during operational exercises considered appropriate during their time are now considered unethical. Nevertheless, research using human subjects remains mission essential in a wide variety of operational, medical, and research, development, testing and evaluation settings. Human use research encompasses a broad range of endeavors, some of which are not commonly recognized as research (see definition of Research). Support from all echelons is required to protect the rights and safety of the volunteer subject.

5. Definitions. Terms used in this instruction are defined by references (a), (b), (c), and (h), except as modified in enclosure (1).

6. Policy

a. Guiding Principles

(1) Protection of human subjects shall be viewed as an important command issue at all echelons, both ashore and afloat. Commanders, commanding officers, officers in charge, heads of activities, scientific and technical program managers, project directors and investigators must maintain concern for the safety and ethical use of volunteer subjects.

(2) Studies involving human subjects must have reasonable prospects of contributing to human benefit and of yielding important results that are not obtainable by other methods. Research involving human subjects shall be scientifically sound and designed to minimize risk. The anticipated benefit shall clearly justify the risk incurred by the subjects. The number of human subjects used shall be kept to the minimum necessary to test appropriately a question or hypothesis.

(3) When applicable, sufficient preliminary animal or laboratory experiments must be completed to minimize the risk of any proposed research involving human subjects.

(4) The rights, welfare, interests, privacy and safety of the human subject shall be held paramount at all times, and all projects must be conducted in a manner that avoids all unnecessary physical or mental discomfort, and economic, social or cultural harm.

(5) Due to the possibility of injuries arising from participation in human subject research, every project involving more than minimal risk shall include an arrangement for treatment and necessary follow-up of any research-related injury in addition to providing emergent treatment. Such arrangement may be that all subjects are eligible Department of Defense (DoD) healthcare beneficiaries, that they are granted secretarial designation as DoD healthcare beneficiaries, or that specific obligations for such treatment have otherwise been made.

(6) No human subject research shall be conducted until the organization performing the research meets all the provisions of this instruction.

(7) Studies involving protected classes of human subjects such as fetuses, pregnant women, human in vitro fertilization, prisoners, and children shall only be conducted following reference (b). Subjects enrolled in an approved study who are imprisoned for whatever reason shall be disenrolled from the study in the most expeditious manner commensurate with their safety.

(8) Voluntary informed consent is fundamental to ethical human use research. It is not simply a document. It is a process that begins with subject recruitment. Informed consent includes a full discussion of the nature of the study between scientifically competent persons and the prospective subjects and/or their legally authorized representatives and continues for at least the duration of the research. Depending on the nature, type and duration of the research, ongoing discussion with and education of subjects about the study may continue long after the original informed consent is obtained.

b. Review, Approval, and Performance of Human Use Research

(1) Reference (c) specifically separates Institutional Review Boards (IRB) review from protocol approval. DON IRBs shall not approve protocols but advise the Approval authority. However, the IRB Chair may be delegated Approval authority for expedited review as defined in Section 110 of reference (a).

(2) No study involving human subjects shall be initiated nor shall subjects be solicited or enrolled until the protocol has been favorably reviewed by an IRB and approved per reference (c). Second-level review shall be provided for all protocols, including studies categorized as exempt according to Section 101(b) of reference (a), following local review. It is unnecessary to wait for completion of the Second-level Review before initiating the study.

(3) All naval commands or activities shall hold an Institutional Assurance from a DON Assurance Issuing Authority before conducting or engaging in human use research. Non-naval activities engaged in human use research must hold either a DoD assurance or an assurance from the Office of Human Research Protection, Department of Health and Human Services (HHS), per Section 103 of reference (b).

(4) IRBs at DON activities perform a Government, and not merely an advisory, function in the approval process. Members shall be either Federal employees, or consultants consistent with the requirements established per reference (d).

(5) No person shall be involved in any review or approval of a protocol when there may be an apparent, actual, or potential conflict of interest, except to provide information requested by the IRB. Any project for which the commander, commanding officer, head of the DON activity, or Approving Official is also an investigator shall be approved at a higher echelon of command, with Approval authority.

(6) Safeguards or special conditions recommended by the IRB shall not be reduced by the Approving Official, nor shall a protocol be approved that has been recommended for disapproval by the IRB.

(7) In the case of studies intending to use investigational new drugs, biologicals or medical devices, IRB membership shall include at least one physician. The physician member may be either a regular or an ad hoc member.

(8) Investigators or research staff may install, familiarize themselves with, calibrate or exercise research equipment, in preparation for the research effort, prior to IRB review.

(9) Familiarization or training of persons who may become research subjects is considered part of the research and shall only be conducted after the protocol has been approved and the subject has provided informed consent.

(10) Investigators may act as subjects in their research only after approval of the protocol and provision of informed consent. Additionally, in the case of greater than minimal risk research, the specific concurrence of the IRB is required.

(11) A joint review agreement may be negotiated among participating activities with the intention of minimizing duplication and speeding approval without sacrificing any of the protections of human subjects in accordance with Sections 103 and 114 of reference (a). Each component of the study file should be managed in accordance with the respective institution's policy regarding the manner and duration of storage.

c. Informed Consent

(1) Informed consent must be obtained and documented following reference (f) and Sections 116 and 117 of reference (a) prior to the involvement of the subject in the research. The requirement to obtain a signed informed consent document may only be waived with a specific IRB determination consistent with Section 117(c) of reference (a).

(2) For research involving any person without the legal capacity to provide consent (that is, for all children and for any adult with compromised capability to give informed consent), participation in research is only authorized when the prospective subject is intended to benefit from the research per reference (f), and subpart D of reference (b) in the case of children.

(3) For research involving adults who may have compromised competence, the protocol shall specify the method for determining the intended subject's legal competence. When an incompetent subject regains competence, direct informed consent must be obtained from the subject for continued participation in the protocol or the subject must be disenrolled.

(4) An investigator shall provide the prospective subject or the subject's legal representative sufficient opportunity to consider whether or not to participate voluntarily, an adequate opportunity to understand the consent document, and enough time to have questions answered. All information provided to the prospective subject or the subject's legal representative shall be presented in language understandable to that individual.

(5) The informed consent document shall not include exculpatory language waiving or appearing to waive any of the subject's legal rights, or releasing or appearing to release the investigator, the sponsor, the institution or its agents from liability for negligence.

(6) The informed consent document shall include text that discusses the risks to the subject and any costs that may be incurred as a consequence of participation in the study.

(7) In all cases, the subject or the subject's legal representative shall be made aware of the provisions of reference (g), and an appropriate Privacy Act statement shall be included with the consent document.

(8) The informed consent document shall be signed and dated by the subject or subject's legal representative, the

individual(s) authorized by the IRB to obtain the consent, and the witness, if required.

(9) All signatures on informed consent documents shall be performed in the presence of a witness when the research involves greater than minimal risk or when oral consent is used in accordance with Section 117(b)(2) of reference (a). The witness shall not be involved in the study or related to the subject. The witness' signature is intended to attest that the information in the consent document and any other written information was explained to and apparently understood by the subject or the subject's legal representative, that questions and concerns were addressed, and that informed consent was freely given.

(10) In the case of exceptional circumstances, such as physical disability precluding signature by an otherwise competent subject, the IRB will determine appropriate means for documenting the consent process, following the policies of Section 117 of reference (a).

(11) DON IRB records and DON completed original signed informed consent documents (or records documenting oral consent per Section 117 of reference (a)) shall be considered "Project Case Files" and retained permanently following reference (e).

d. Studies Involving the Use of Investigational Agents. All studies involving the use of Investigational Agents shall follow the guidance of reference (h).

e. International Studies. When research is conducted outside the United States involving the use of human subjects, the laws, customs and practices of the country in which research is conducted, or those required by this instruction, whichever are more stringent, shall take precedence. The research shall meet the same standards of ethics and safety that apply to research conducted within the United States.

7. Responsibilities

a. The Assistant Secretary of the Navy (Research, Development and Acquisition) (ASN(RD&A)) shall:

(1) Ensure development of policies and programs for the safe and ethical use of human subjects in naval research in coordination with the Office of the Director, Marine Corps Staff.

These policies and programs shall provide for the responsible conduct of research, including:

(a) Education and training of all personnel who review, approve, perform, and manage research involving human subjects,

(b) Ethical review, and

(c) Compliance.

(2) Endorse and forward to the Director, Defense Research and Engineering for approval of all studies involving actual exposure of human subjects to the effects of nuclear, biological, or chemical warfare agents or weapons.

(3) Serve as the Approving Official for any research involving:

(a) Severe or unusual intrusions, either physical or psychological, on the human subject (e.g., consciousness-altering drugs, mind-control techniques, abnormal environments involving extreme risk),

(b) Prisoners, or

(c) Potential political or public embarrassment to the DON.

(4) Ensure availability of ASN(RD&A) staff expertise in the protection of human subjects in research.

b. The Chief of Naval Operations (Surgeon General (SG) of the Navy (N093)) is:

(1) Delegated authority to issue DoD Institutional Assurances to all naval activities. The SG is also delegated authority to issue DoD Institutional Assurances to contractors conducting research using human subjects as described in paragraph 3a of this instruction, except as specifically assigned to the Chief of Naval Research (CNR). All studies using Navy or Marine Corps personnel or employees of the DON as subjects fall under the purview of the SG. This authority may be delegated but not further subdelegated.

(2) Designated the Approving Official for all naval research using human subjects except for research under the Approval authority of the CNR or research requiring approval by higher authority. The SG may further delegate Approval authority

to Navy Assurance Issuing Authorities. This Approval authority may be further delegated.

c. The CNR is:

(1) Delegated authority to issue DoD Institutional Assurances to all contractors conducting research using human subjects in studies that do not include Navy or Marine Corps personnel or employees of the DON as subjects, and that are funded or sponsored by the Office of Naval Research. This authority may be delegated but not further subdelegated.

(2) Designated the Approving Official for research using human subjects in studies specified in paragraph 7c(1). This Approval authority may be further delegated to offices responsible for Second-level Review.

d. Assurance Issuing Offices shall:

(1) Provide guidance and consultation regarding the implementation of this instruction.

(2) Negotiate and issue numbered DoD Institutional Assurances.

(3) Establish appropriate monitoring procedures to determine if institutions under their purview remain in compliance with the terms of their Institutional Assurance.

(4) Provide Second-level Review for all protocols from institutions under their purview, including studies categorized as exempt according to Section 101(b) of reference (a). Second-level Review shall be accomplished regardless of whether the research is performed under a DoD or HHS Assurance.

(5) Approve, before implementation, requests from performing institutions to enter into joint review arrangements.

(6) Not further subdelegate any of the above responsibilities.

(7) Delegate, as appropriate, to the commander, commanding officer, or head of a DON activity the authority to approve the use of human subjects in research. Recipients of delegated Approval authority from an Assurance Issuing office may

not subdelegate this authority except to permit IRB chairs to approve research using expedited procedures.

e. Commanders/commanding officers/heads of naval activities whose involvement with a specific research protocol is limited to permitting outside investigators to recruit personnel as subjects onboard their command, shall require Certification(s) from the performing activity or activities before allowing participation of their personnel. This responsibility extends to commanders/ commanding officers/heads of all naval activities, including vessels afloat, training commands and Marine units.

f. Commanders/commanding officers/heads of naval activities engaged in research shall:

(1) Establish an IRB following references (a) and (c) or negotiate a formal agreement with an external IRB at another institution that holds an appropriate assurance.

(2) Obtain an Institutional Assurance, appropriate for the research in question, from the activity's Assurance Issuing Authority or provide evidence of an appropriate HHS Assurance before conducting research using human subjects.

(3) Serve as their activity's Approving Official, contingent upon holding delegated Approval authority. Subdelegation is authorized only to the Chair of the IRB for expedited review as set forth in paragraph 7d(7) above.

(4) Issue Certifications to funding sponsors following Section 103(f) of reference (a).

(5) Provide the activity's Assurance Issuing Authority with documents for Second-level Review within 15 working days after approval.

(6) Maintain research records as "Project Case Files" following reference (e).

(7) Allocate adequate resources including but not limited to logistical, financial, and educational resources, to ensure compliance with the activity's Institutional Assurance and all applicable guidance.

(8) In cooperative/collaborative research projects, negotiate an agreement with the other participating institution(s) that includes at a minimum a statement of work and a specific assignment of responsibilities. This assignment must

include at least responsibility for IRB review, oversight, reporting, and compliance for the project as a whole, as well as record keeping, reporting, ongoing monitoring and compliance at each site of performance. In cases of proposed assignment of primary IRB responsibility to another institution, the commanding officer shall obtain the approval of the activity's Assurance Issuing Authority as set forth in paragraph 7d(5) of this instruction prior to finalizing the agreement. All cooperative research still requires specific DON approval and Second-level Review.

(9) Verify that a contractor applying for support holds a valid HHS or DoD Institutional Assurance and has submitted a Certification executed by an individual authorized to act for that organization.

g. Naval Approving Officials shall:

(1) Not approve a protocol that has been recommended for disapproval by the IRB.

(2) Not reduce the safeguards or conditions recommended by the IRB.

(3) Determine whether to approve or disapprove the protocol, require additional safeguards, or refer the protocol to a higher Approval authority. When determining whether to approve the proposed research, the Approving Official shall review and consider, at a minimum, the signed minutes of IRB meetings.

h. Naval IRBs shall:

(1) Determine the applicability of this instruction to all protocols presented for review, including determination of exempt research.

(2) Establish the level of risk involved in a particular protocol.

(3) Following reference (c), approve an appropriate health care provider to be the medical monitor for all research categorized as greater than minimal risk. IRBs will ensure that the role(s) of the monitor during subject selection, enrollment, participation, and/or follow-up have been specified in writing. The monitor shall not be an investigator on that research study.

(4) Ensure that safety-monitoring plans are implemented proportionate to risk following reference (c).

(5) Conduct continuing review of all approved studies at least once a year, or more often, as warranted by the level of risk.

(6) Provide timely notification to the Approving Official of all issues of safety or incidents of non-compliance with this instruction and other relevant guidance and directives.

(7) Ensure that the study shall be conducted only by investigators possessing the requisite human use training and relevant scientific qualifications.

i. Chairs of Naval IRBs shall:

(1) Have delegated authority from the Approving Official to suspend a previously approved research project when there is any significant deviation from the protocol, any serious adverse event, or for other reasonable cause.

(2) Ensure that the IRB is informed of all actions taken under expedited review authority.

j. Principal Investigators shall:

(1) Have primary responsibility for compliance with all provisions of this instruction and the protection of human subjects regulations.

(2) Submit all proposals that may involve research using human subjects, even those thought to be exempt under Section 101(b) of reference (a), to the IRB for determination of the applicability of this instruction.

(3) Provide a written Investigator's Assurance for compliance with all applicable laws, regulations, policies and directives for all designated investigators on a specific study.

(4) Submit all proposed changes to an approved study to the IRB for review and approval prior to implementation.

(5) In the case of research involving greater than minimal risk of physical harm, make provision in the protocol for the rapid medical evacuation of subjects to an adequate treatment facility in case of need.

(6) Notify an affected subject as soon as feasible of any serious adverse event.

(7) Notify the IRB Chair within 24 hours of any unanticipated serious adverse event.

(8) Notify the IRB Chair of any deviation from the approved protocol as soon as possible. Identify causes, and submit a protocol amendment to the IRB that addresses the problems that led to the deviation.

(9) Provide a summary of all adverse events to the IRB at each continuing review and at the conclusion of the research project.

(10) Provide subjects or their legally authorized representative with a copy of the completed informed consent document except for those studies qualifying for waiver of documentation of informed consent per Section 117 of reference (a). For greater than minimal risk research, in the case of a DoD beneficiary, a copy shall also be forwarded to the subject's medical records custodian, and for a non-DoD beneficiary, a second copy shall be provided to the individual subject for inclusion in the subject's personal medical records.

(11) Suspend a subject's participation at any time if there is reason to suspect that continuation is likely to result in harm, disability or death. This responsibility extends to every member of the investigative team.

k. Any specific situations not addressed in this instruction should be referred to the SG for clarification.

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DEFINITIONS

1. Adverse Event. Any unfavorable and unintended occurrence associated with the conduct of a research project.

2. Approval. Specifically delegated authority to accept the recommendation of an IRB.

3. Approving Official. An individual with delegated Approval authority. Such individual may or may not also have authority to certify a research protocol.

4. Assurance Issuing Authority. An office authorized to issue Institutional Assurance numbers to DON activities and contractors performing human subjects research.

5. Certification. The formal written notification by the performing activity that a human subject research protocol has been properly reviewed and approved by an IRB specified in the activity's assurance, and that participation is within the bounds of the activity's assurance.

6. Contractor. Any individual or organization that is a party to a contract, grant, interagency transfer or other agreement with any Navy or Marine Corps activity. An organization includes any Federal, State, municipal or other Government activity, or any corporation, institution, foundation, agency, or other legal entity, whether foreign or domestic.

7. Engaged in Research. An activity becomes engaged in research when its personnel or agents either (a) intervene or interact with living individuals for research purposes; or (b) obtain individually identifiable private information for research purposes.

8. Institutional Assurance. A written document originated by the performing institution to be considered by the Assurance Issuing Authority which states that the performing institution will comply with the requirements of reference (a) for a specific project or category of research.

9. Investigational Agents. Drugs, biologicals, and devices as defined by reference (h).

10. Investigator's Assurance. A pledge signed by all investigators in which they acknowledge their responsibilities for the protection of human subjects.